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ORIGINAL RESEARCH

Epidemiology of Reportable Bacterial Infectious Diseases in Saudi Arabia

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ABSTRACT

Introduction: Bacterial infections have a significant impact on human health; they can cause severe morbidity and mortality, particularly in susceptible populations. Epidemiological surveillance is a critical tool for monitoring the population's health and facilitate the prevention and control of infectious disease outbreaks. Knowing the burden of bacterial communicable diseases is an initial core step toward public health goals.

Methods: Saudi epidemiology surveillance data were utilized to depict the changing epidemiology of bacterial infectious diseases in Saudi

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Arabia from 2018 to 2021. The cumulative numbers of cases, demographics, and incidence rates were analyzed and visualized. Parametric tests were used to compare the difference in the mean values between categorical variables. Regression analysis was employed to estimate trends in disease rates over time. Statistical significance was set at p value ≤ 0.05.

Results: The results revealed that brucellosis, tuberculosis, and salmonellosis were the most frequently reported bacterial infectious diseases in Saudi Arabia. Males were more significantly affected by brucellosis and tuberculosis infections than females. Salmonellosis infections were more significant among Saudi citizens, while pulmonary tuberculosis was more significant in non-Saudis. Interestingly, there was a decline in the incidence rates of numerous bacterial infectious diseases during the Coronavirus Disease 2019 (COVID-19) pandemic and COVID-19 restrictions. Some bacterial infectious diseases were rarely reported in Saudi Arabia, including syphilis and diphtheria.

Conclusions: The future perspective of this research is to enhance disease surveillance reporting by including different variables, such as the source of infection, travel history, hospitalization, and mortality rates. The aim is to improve the sensitivity and specificity of surveillance data and focus on the mortality associated with bacterial pathogens to identify the most significant threats and set a public health priority.

Keywords: Bacterial infections; Surveillance; Epidemiology; Prevention; Saudi Arabia

Key Summary Points

Why carry out the study?

Bacterial infections are well known as one of the leading causes of global infection-related morbidity and mortality.

Epidemiological surveillance is a critical tool for monitoring the population's health and facilitate the prevention and control of infectious disease outbreaks.

This study aims to highlight the current Saudi epidemiology surveillance data and describe the bacterial infectious diseases reported in the Kingdom between 2018 and 2021.

What was learned from the study?

The results revealed that brucellosis, tuberculosis, and salmonellosis were the most frequently reported bacterial infectious diseases in Saudi Arabia, while some bacterial infectious diseases were rarely reported, including syphilis and diphtheria.

There was a significant difference in the distribution of some bacterial infectious diseases between Saudi and non-Saudi citizens and between males and females.

The study revealed multiple opportunities for enhancement in the Saudi surveillance system; implementing an improved public health surveillance system helps overcome challenges associated with controlling infectious diseases.

INTRODUCTION

Infectious diseases have long been recognized as a leading cause of illness and death and a global priority for public health [1]. According to the World Health Organization (WHO), lower respiratory infections and diarrheal diseases were among the top 10 leading causes of death worldwide [2]. Bacterial infections are remarkably involved in global infection-related deaths; however, more data are needed to present a comprehensive global estimate of mortality associated with bacterial infections. In a recent study that estimated global mortality, 13.6% of all global deaths and 56.2% of all sepsis-related deaths were due to 33 bacterial pathogens. The leading bacterial pathogens associated with global death are *Staphylococcus* *aureus*, *Escherichia coli*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* [3]. The United States Centers for Disease Control and Prevention (CDC) established the Active Bacterial Core surveillance, which provides estimates on invasive bacterial infections of public health importance in the United States (US) and offers the infrastructure to track disease trends and facilitate public health research [4]. In Saudi Arabia, epidemiologic data on bacterial infections are crucial to implement targeted prevention efforts. This is particularly important as each year the country hosts millions of pilgrims from all over the world that arrive in the country to perform Hajj and Umrah [5]. During the Hajj and Umrah seasons, the potential for infectious disease outbreaks is remarkably high due to the crowded conditions [6]. However, Saudi Arabia has shown remarkable achievements in reducing the burden of disease and improving the access and quality of health care in recent years. It has also invested in strengthening its public health systems and building capacity for disease outbreak response, surveillance, laboratory systems, and workforce development. Furthermore, it has implemented various preventive and control measures such as vaccination campaigns, screening programs, antimicrobial stewardship programs, and public awareness campaigns [7].

Monitoring the burden of infectious diseases and their epidemiology is crucial for maintaining the population's health by controlling disease outbreaks and facilitating disease prevention. In Saudi Arabia, the Field Epidemiology Program & Surveillance and Data Management unit of the Ministry of Health is responsible for tracking infectious diseases. National surveillance data are essential in tracking trends in disease rates and, most importantly, the impact of control measures such as vaccination programs in eliminating and eradicating certain infectious diseases [8]. Knowing the burden of bacterial communicable diseases is an initial core step toward public health. Therefore, this study aims to highlight the current Saudi epidemiology surveillance data of bacterial infectious diseases in the Kingdom of Saudi Arabia reported between 2018 and 2021.

METHODS

The Saudi epidemiology surveillance system collects and aggregates data on a national level using the "HESN" program, a public health solution for disease surveillance and management. The data sources include laboratories, primary healthcare, hospitals, and specific health programs. The case definitions for the surveillance data are categorized as *possible* based on clinical criteria, *probable* based on clinical criteria, epidemiological link, and presumptive laboratory criteria, and *confirmed* based on laboratory confirmation. Among bacterial diseases, tuberculosis can be reported as possible, and brucellosis, meningococcal infections, pertussis, syphilis, and tetanus can be reported as probable. The International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) is utilized for diagnosis coding by the Ministry of Health in Saudi Arabia [9].

In this study, the Saudi surveillance data were utilized to depict the changing epidemiology of bacterial infectious diseases in Saudi Arabia from 2018 to 2021, along with a detailed graphical analysis of the cases during the same period. The cumulative cases and demographics (sex, nationality, and age) were calculated and reported. Sex is defined as male and female; nationality is classified as Saudi and non-Saudi; age groups are categorized as 0–4 age group, 5–14 age group, 15–29 age group, 30–59 age group, and elderly (60 years and above). For each disease, the incidence rates per 100,000 population were calculated with a 95% confidence interval, and population data for 2018–2021 years were used. To compare the difference in the mean values between categorical variables such as sex and nationality, Student's *t* test was employed since the data were normally distributed. One-way ANOVA analysis was used to test for differences in the mean values between different age groups (normally distributed). If the results revealed statistical significance between the age groups, post hoc analysis was conducted using Bonferroni correction. Regression analysis was employed to estimate trends in disease rates over time. Data analyses were performed using Microsoft Excel software (version 16.75.2). Statistical significance was set at p value ≤ 0.05. These data describe the incidence of bacterial infectious diseases over time and the differences among groups for each characteristic. This study is based on previously collected data and does not contain any new data that involved human participants or animals performed by any of the authors.

RESULTS

In Saudi Arabia, 13 bacterial infectious diseases are included in the Saudi epidemiology surveillance. These infections include brucellosis, TB (both pulmonary and extra-pulmonary), Salmonellosis, typhoid and paratyphoid fever, meningitis, shigellosis, pertussis, cholera, tetanus, leprosy, *Haemophilus influenzae* (encephalitis), syphilis, and diphtheria. The most common reportable bacterial infection in Saudi Arabia is brucellosis, followed by tuberculosis (both pulmonary and extrapulmonary), and Salmonellosis. Table 1 shows a summary of the reportable cases in Saudi Arabia from 2018 to 2021. Table 2 summarizes the differences in mean values of categorical variables (sex and nationality), while Table 3 summarizes the differences in mean values between different age groups throughout the study period. Table 4 shows the results of regression analysis of bacterial infectious disease trends over time.

Brucellosis is a widespread zoonotic infection caused by Gram-negative bacteria of the *Brucella* species [10]. Brucellosis was the most reported bacterial infectious disease in Saudi Arabia between 2018 and 2019 (Table 1). In 2018, brucellosis incidence rate was 17.3 (95% CI: 17.16, 17.44). Then, brucellosis incidence during 2019 decreased slightly to 14.0 (95% CI: 13.87, 14.13). Interestingly, cases dropped remarkably in 2020 and 2021, with a rate of 7.3 (95% CI: 7.19, 7.41) and a rate of 7.1 (95% CI: 7.04, 7.16), respectively. Fortunately, a significant decreasing trend in brucellosis incidence rate was observed (p value = 0.04). Brucellosis affected males more significantly than females (p value = 0.04). There was a significant difference in the average brucellosis cases between different age groups (p value < 0.01). However, post hoc analysis revealed no statistical significance.

Tuberculosis (TB) is one of the most reported bacterial infectious diseases in Saudi Arabia, where more than 2000 people get infected with pulmonary TB yearly, while *Extrapulmonary tuberculosis* (EPTB) cases range from 600 to 900 annually (Table 1). In 2018, the incidence rate of TB was 12.9 (95% CI: 12.82, 12.98). The TB incidence decreased from 12.0 (95% CI: 11.95, 12.05) in 2019 to 8.6 (95% CI: 8.51, 8.69) in 2020. However, the incidence of TB increased to 10.2 (95% CI: 10.11, 10.29) during 2021. The incidence of pulmonary TB is significantly higher among non-Saudi than Saudi citizens (p value = 0.01). TB affected males more significantly than females (pulmonary TB p value < 0.01, EPTB p value = 0.01). Most of the TB infections in Saudi Arabia affect adults more than children. Post hoc analysis revealed that TB infections (both pulmonary TB and EPTB) were significantly higher in 15-year-old and above age groups than in 0–4 and 5–14 age groups (p value < 0.005). Pulmonary TB and EPTB in the elderly (60 and above) were significantly lower than in the 30–59 age group (p value = 0.005). Pulmonary TB incidence was substantially higher in the 15–29 age group than in the elderly (60 and above), with a p value < 0.005.

Salmonellosis is one of the four global causes of diarrheal diseases [11]. It is one of the most highly reported bacterial infectious diseases in Saudi Arabia, where around 2000 people become infected annually (Table 1). In 2018, the salmonellosis incidence rate was 6.8 (95% CI: 6.69, 6.91) in Saudi Arabia. The incidence increased to 8.5 (95% CI: 8.39, 8.61) in 2019. In 2020, there was a remarkable decline in salmonellosis incidence rate to 4.6 (95% CI: 4.52, 4.68). However, in 2021, salmonellosis incidence increased remarkably to 7.2 (95% CI: 7.09, 7.31). *S. salmonellosis* was reported in Saudi citizens more significantly than non-Saudis (p value = 0.01). There was a significant difference in the average salmonellosis cases between different age groups (p value < 0.01). Post hoc analysis revealed that children under the age of 5 were more significantly affected by salmonellosis compared with the 5–14 age group (p value = 0.004), 15–29 age

Table 1 The total number of reported bacterial infectious diseases (2018–2021) in Saudi Arabia

Bacterial infectious disease	Total in 2018 (IR[a])	95% CI	Total in 2019 (IR[a])	95% CI	Total in 2020 (IR[a])	95% CI	Total in 2021 (IR[a])	95% CI
Brucellosis	5213 (17.3)	17.16–17.4	4219 (14.0)	13.87–14.13	2302 (7.3)	7.19–7.41	2193 (7.1)	7.04–7.16
Tuberculosis (TB)	3907 (12.9)	12.82–13.0	3596 (12.0)	11.95–12.05	2717 (8.6)	8.51–8.69	3154 (10.2)	10.1–10.29
Pulmonary TB	2991 (9.9)	9.82–9.98	2751 (9.2)	9.16 -9.24	2109 (6.7)	6.63–6.77	2393 (7.8)	7.73–7.87
EPTB	916 (3.0)	2.98–3.02	846 (2.8)	2.78–2.82	608 (1.9)	1.88–1.92	761 (2.5)	2.47 -2.53
Salmonella infection	2061 (6.8)	6.69–6.91	2568 (8.5)	8.39–8.61	1450 (4.6)	4.52–4.68	2208 (7.2)	7.09–7.31
Typhoid–paratyphoid fever	391 (1.3)	1.29–1.31	612 (2.0)	1.97–2.03	287 (0.9)	0.88–0.92	277 (0.9)	0.88–0.92
Meningitis	228 (0.8)	0.79–0.81	246 (0.8)	0.79–0.81	123 (0.4)	0.39–0.41	94 (0.3)	0.29–0.31
Meningitis meningococcal	5 (0.02)	0.02–0.02	6 (0.02)	0.02–0.02	8 (0.03)	0.03–0.03	8 (0.03)	0.03–0.03
Meningococcemia	0 (0.0)	0	2 (0.01)	0.01–0.01	1 (0.0)	0	1 (0.0)	0
Meningitis—pneumococcal	27 (0.09)	0.09–0.09	29 (0.1)	0.1–0.1	6 (0.02)	0.02–0.02	5 (0.02)	0.02–0.02
Meningitis—HIB	10 (0.03)	0.03 0.03	5 (0.02)	0.02–0.02	1 (0.0)	0	1 (0.0)	0
Meningitis—other	186 (0.6)	0.59–0.61	204 (0.7)	0.69–0.71	107 (0.3)	0.29–0.31	79 (0.3)	0.29–0.31
Pertussis	24 (0.1)	0.1–0.1	207 (0.7)	0.68–0.72	77 (0.2)	0.19–0.21	29 (0.1)	0.1–0.1
Shigellosis	68 (0.23)	0.22–0.24	75 (0.25)	0.24–0.26	36 (0.11)	0.11–0.11	54 (0.18)	0.18–0.18
Cholera	53 (0.2)	0.19—0.21	41 (0.1)	0.09–0.11	12 (0.04)	0.04–0.04	14 (0.05)	0.05–0.05
Cholera—O1	41 (0.1)	0.09–0.11	30 (0.1)	0.1–0.1	4 (0.01)	0.01–0.01	3 (0.01)	0.01–0.01

Table 1 continued

Bacterial infectious disease	Total in 2018 (IR[a])	95% CI	Total in 2019 (IR[a])	95% CI	Total in 2020 (IR[a])	95% CI	Total in 2021 (IR[a])	95% CI
Cholera—O139	0 (0.0)	0	0 (0.0)	0	2 (0.01)	0.01–0.01	0 (0.0)	0
Cholera—non-O1 non-O139	12 (0.04)	0.04–0.04	11 (0.04)	0.04–0.04	6 (0.02)	0.02–0.02	11 (0.04)	0.04–0.04
Tetanus	16 (0.05)	0.05–0.05	30 (0.1)	0.1–0.1	15 (0.05)	0.05–0.05	10 (0.03)	0.03–0.03
Non-neonatal tetanus	12 (0.04)	0.04–0.04	22 (0.07)	0.07–0.07	13 (0.04)	0.04–0.04	5 (0.02)	0.02–0.02
Neonatal tetanus	4 (0.01)	0.01–0.01	8 (0.03)	0.03–0.03	2 (0.01)	0.01–0.01	5 (0.02)	0.02–0.02
Leprosy	29 (0.1)	0.1–0.1	17 (0.06)	0.06–0.06	14 (0.04)	0.04–0.04	20 (0.06)	0.06–0.06
HIB: encephalitis	2 (0.01)	0.01–0.01	1 (0.0)	0	1 (0.0)	0	1 (0.0)	0
Syphilis	0 (0.0)	0	0 (0.0)	0	9 (0.03)	0.03–0.03	0 (0.0)	0
Diphtheria	1 (0.0)	0	2 (0.01)	0.01–0.01	0 (0.0)	0	0 (0.0)	0

IR incidence rate, *CI* confidence interval, *EPTB* extrapulmonary tuberculosis, *HIB Haemophilus influenzae* type B

[a] Incidence rate per 100,000 population

group (p value = 0.002), and 60 years and above age group (p value = 0.004).

Typhoid and paratyphoid fever (enteric fever) are types of *Salmonella* infections that are clinically different from common salmonellosis [12]. Typhoid and paratyphoid fever affects around 300 individuals annually in Saudi Arabia (Table 1). In 2019, typhoid and paratyphoid fever incidence rate increased from 2.0 (95% CI: 1.97, 2.03) compared to the rate of previous year 1.3 (95% CI: 1.29, 1.31), subsequently dropping by half in 2020 and 2021 with a rate of 0.9 (95% CI: 0.88, 0.92) for both 2 years. However, no significant decreasing trend was observed. There was a significant difference in the average typhoid and paratyphoid fever cases between different age groups (p value < 0.01). However, post hoc analysis revealed no statistical significance.

Bacterial meningitis has the highest global burden and remains a significant public health challenge [13]. Among all bacteria, *N. meningitidis* has the potential to spread rapidly, leading to large epidemics [13]. *Meningococcal meningitis* is relatively rare in Saudi Arabia, as each year around seven cases of meningococcal meningitis are reported (Table 1). During 2018–2019, the incidence of meningococcal meningitis was 0.02 cases per 100,000 persons; then the incidence increased slightly to 0.03 during 2020–2021. A significant increasing trend in meningococcal meningitis incidence rate was observed (p value

Table 2 The difference in the mean values between categorical variables (sex and nationality) for each reported bacterial infection in Saudi Arabia

Bacterial infectious disease	Reported sex			Reported nationality		
	Male (mean)	Female (mean)	*p* value	Saudi (mean)	Non-Saudi (mean)	*p* value
Brucellosis	2662.50	818.25	**0.04**	2342.25	1114.75	0.08
Pulmonary TB	1794.50	765.00	**0.002**	1012.25	1529.75	**0.01**
Extra-pulmonary TB	527.50	254.50	**0.01**	347.25	432.25	0.14
Salmonella infection	1108.50	962.50	0.41	1527.50	519.25	**0.01**
Typhoid-paratyphoid fever	247.75	143.75	0.15	162.75	217.25	0.41
Meningitis meningococcal	4.00	2.75	0.36	4.75	2.00	0.07
Meningococcemia	0.75	0.25	0.21	0.75	0.00	0.22
Meningitis—pneumococcal	10.00	6.75	0.51	11.75	5.00	0.22
Meningitis—HIB	2.75	1.50	0.46	4.00	0.25	0.15
Meningitis—other	83.25	60.75	0.35	106.75	35.75	**0.04**
Pertussis	38.00	46.25	0.79	75.50	8.00	0.19
Shigellosis	30.25	28.00	0.76	43.50	13.75	**0.01**
Cholera—O1	14.50	5.00	0.29	2.00	17.25	0.21
Cholera—O139	0.25	0.25	1.00	0.25	0.25	1.00
Cholera—non-O1 non-O139	6.25	3.75	0.14	6.25	3.75	0.3
Non-neonatal tetanus	12.50	0.50	**0.03**	1.75	11.00	**0.03**
Neonatal tetanus	3.50	1.25	0.1	0.50	4.50	**0.03**
Leprosy	15.25	4.75	**0.04**	4.25	15.75	**0.01**
HIB: encephalitis	1.00	0.00	0.09	1.00	0.00	0.09
Syphilis	2.00	0.25	0.45	1.50	0.50	0.56
Diphtheria	0.50	0.25	0.54	0.25	0.50	0.54

The bolded values represent the statistically significant values (p value ≤ 0.05)

EPTB extrapulmonary tuberculosis; *HIB Haemophilus influenzae* type B

= 0.05). This increasing trend is concerning, especially during the Hajj and Umrah seasons. In 2021, only one case of *meningococcemia* (a rare infectious disease caused by *N. meningitidis*) was reported in Saudi Arabia (Table 1). *Pneumococcal meningitis* refers to meningitis caused by S. *pneumoniae*. Pneumococcal meningitis incidence is relatively low in Saudi Arabia (Table 1). Interestingly, meningitis-pneumococcal incidence remarkably dropped from 0.09 cases per 100,000 persons in 2018 to 0.02 in 2021. *Haemophilus meningitis* is a form of meningitis caused by *H. influenzae*, usually *H. influenzae* type B (HIB). In Saudi Arabia, ten confirmed cases of *Haemophilus meningitis* were reported in 2018, with a rate of 0.03 cases per 100,000 persons (Table 1). In 2019, the number of reported cases dropped to 5 (a rate of 0.02 cases per 100,000 persons) and continued to decrease to one reported case in 2020 and 2021. The Saudi epidemiological

Table 3 One-way ANOVA tests on different age groups for each reported bacterial infection in Saudi Arabia

Variables	Age groups	Count	Sum	Average	Variance	*F*	*p* value
Brucellosis	0–4	4.00	459.00	114.75	2990.25	9.90	**0.00**
	5–14	4.00	1555.00	388.75	27834.25		
	15–29	4.00	3550.00	887.50	196352.33		
	30–59	4.00	6606.00	1651.50	484579.00		
	60 and above	4.00	1710.00	427.50	22857.00		
Pulmonary TB	0–4	4.00	137.00	34.25	108.92	115.54	**0.00**
	5–14	4.00	147.00	36.75	37.58		
	15–29	4.00	3565.00	891.25	27333.58		
	30–59	4.00	5165.00	1291.25	22154.25		
	60 and above	4.00	1224.00	306.00	4358.00		
Extra-pulmonary tuberculosis	0–4	4.00	79.00	19.75	58.92	76.05	**0.00**
	5–14	4.00	98.00	24.50	21.67		
	15–29	4.00	1139.00	284.75	4183.58		
	30–59	4.00	1488.00	372.00	2364.00		
	60 and above	4.00	326.00	81.50	251.00		
Salmonella infection	0–4	4.00	3782.00	945.50	37857.00	29.35	**0.00**
	5–14	4.00	897.00	224.25	1712.25		
	15–29	4.00	1040.00	260.00	10279.33		
	30–59	4.00	1881.00	470.25	18354.92		
	60 and above	4.00	684.00	171.00	702.00		
Typhoid-paratyphoid fever	0–4	4.00	173.00	43.25	1078.25	9.86	**0.00**
	5–14	4.00	253.00	63.25	3058.92		
	15–29	4.00	405.00	101.25	768.25		
	30–59	4.00	681.00	170.25	2502.92		
	60 and above	4.00	53.00	13.25	29.58		
Meningitis—meningococcal	0–4	4.00	9.00	2.25	2.25	1.67	0.21
	5–14	4.00	4.00	1.00	0.67		
	15–29	4.00	4.00	1.00	1.33		
	30–59	4.00	8.00	2.00	2.00		
	60 and above	4.00	2.00	0.50	0.33		

Table 3 continued

Variables	Age groups	Count	Sum	Average	Variance	*F*	*p* value
Meningococcemia	0–4	4.00	1.00	0.25	0.25	1.05	0.41
	5–14	4.00	2.00	0.50	0.33		
	15–29	4.00	0.00	0.00	0.00		
	30–59	4.00	1.00	0.25	0.25		
	60 and above	4.00	0.00	0.00	0.00		
Meningitis—pneumococcal	0–4	4.00	27.00	6.75	14.25	1.73	0.19
	5–14	4.00	9.00	2.25	6.92		
	15–29	4.00	6.00	1.50	5.67		
	30–59	4.00	13.00	3.25	10.25		
	60 and above	4.00	12.00	3.00	10.00		
Meningitis—HIB	0–4	4.00	10.00	2.50	9.00	1.49	0.25
	5–14	4.00	2.00	0.50	1.00		
	15–29	4.00	2.00	0.50	1.00		
	30–59	4.00	2.00	0.50	0.33		
	60 and above	4.00	1.00	0.25	0.25		
Meningitis—other	0–4	4.00	249.00	62.25	741.58	7.76	**0.00**
	5–14	4.00	69.00	17.25	34.92		
	15–29	4.00	69.00	17.25	103.58		
	30–59	4.00	137.00	34.25	168.25		
	60 and above	4.00	52.00	13.00	24.67		
Shigellosis	0–4	4.00	43.00	10.75	30.92	4.42	**0.01**
	5–14	4.00	39.00	9.75	14.92		
	15–29	4.00	50.00	12.50	16.33		
	30–59	4.00	74.00	18.50	15.00		
	60 and above	4.00	27.00	6.75	8.92		
Pertussis	0–4	4.00	295.00	73.75	6408.92	3.18	**0.04**
	5–14	4.00	10.00	2.50	1.67		
	15–29	4.00	5.00	1.25	0.92		
	30–59	4.00	15.00	3.75	10.92		
	60 and above	4.00	7.00	1.75	2.25		

Table 3 continued

Variables	Age groups	Count	Sum	Average	Variance	*F*	*p* value
Cholera—O1	0–4	4.00	2.00	0.50	0.33	1.75	0.19
	5–14	4.00	0.00	0.00	0.00		
	15–29	4.00	42.00	10.50	181.67		
	30–59	4.00	27.00	6.75	53.58		
	60 and above	4.00	7.00	1.75	2.25		
Cholera—O139	0–4	4.00	1.00	0.25	0.25	0.75	0.57
	5–14	4.00	0.00	0.00	0.00		
	15–29	4.00	1.00	0.25	0.25		
	30–59	4.00	0.00	0.00	0.00		
	60 and above	4.00	0.00	0.00	0.00		
Cholera—non-O1 non-O139	0–4	4.00	4.00	1.00	2.00	5.65	**0.01**
	5–14	4.00	3.00	0.75	0.92		
	15–29	4.00	4.00	1.00	0.67		
	30–59	4.00	20.00	5.00	4.67		
	60 and above	4.00	9.00	2.25	2.92		
Non-neonatal tetanus	0–4	4.00	8.00	2.00	2.00	6.49	**0.00**
	5–14	4.00	4.00	1.00	1.33		
	15–29	4.00	8.00	2.00	3.33		
	30–59	4.00	29.00	7.25	14.25		
	60 and above	4.00	3.00	0.75	0.92		
Leprosy	0–4	4.00	1.00	0.25	0.25	13.72	**0.00**
	5–14	4.00	7.00	1.75	4.25		
	15–29	4.00	20.00	5.00	0.67		
	30–59	4.00	45.00	11.25	20.92		
	60 and above	4.00	7.00	1.75	2.25		
HIB: Encephalitis (invasive)	0–4	4.00	0.00	0.00	0.00	1.05	0.41
	5–14	4.00	1.00	0.25	0.25		
	15–29	4.00	1.00	0.25	0.25		
	30–59	4.00	2.00	0.50	0.33		
	60 and above	4.00	0.00	0.00	0.00		

Table 3 continued

Variables	Age groups	Count	Sum	Average	Variance	*F*	*p* value
Syphilis	0–4	4.00	0.00	0.00	0.00	0.64	0.64
	5–14	4.00	0.00	0.00	0.00		
	15–29	4.00	2.00	0.50	1.00		
	30–59	4.00	5.00	1.25	6.25		
	60 and above	4.00	2.00	0.50	1.00		
Diphtheria	0–4	4.00	2.00	0.50	0.33	1.71	0.20
	5–14	4.00	0.00	0.00	0.00		
	15–29	4.00	0.00	0.00	0.00		
	30–59	4.00	1.00	0.25	0.25		
	60 and above	4.00	0.00	0.00	0.00		

EPTB extrapulmonary tuberculosis, *HIB Haemophilus influenzae* type B

surveillance also reports the number of meningitis infections (meningitis-other) caused by other than *N. meningitidis*, *S. pneumoniae*, and *H. meningitis*. However, the report does not specify what "Meningitis-other" includes. *Meningitis-other* incidence is the highest among all cases of meningitis in the Saudi epidemiology report (Table 1). In 2018, the rate of meningitis-other was 0.6 (95% CI: 0.59, 0.61), which declined to 0.3 (95% CI: 0.29, 0.31) in both 2020 and 2021. Meningitis infections caused by other causes were significantly higher among Saudi citizens (p value = 0.04). It is essential to determine the exact cause to monitor the prevalence and epidemiology of all types of meningitis.

Shigellosis is known as the second-leading cause of fatal diarrhea worldwide [14]. Shigellosis in Saudi Arabia was relatively low over the study period from 2018 to 2021 (Table 1). In 2018, the rate of shigellosis was 0.23 (95% CI: 0.22, 0.24). The highest number of shigellosis infections was reported in 2019, with a rate of 0.25 (95% CI: 0.24, 0.26), dropping to 0.11 cases per 100,000 persons in 2020, then slightly increasing to 0.18 cases per 100,000 persons in 2021. Table 2 reveals that shigellosis cases were significantly higher in Saudi than non-Saudi citizens (p value: 0.01). There was a significant difference in the average shigellosis cases between different age groups (p value: 0.01). However, post hoc analysis revealed no statistical significance.

Pertussis remains endemic worldwide, even in countries with high vaccination coverage [15]. Pertussis incidence rates in Saudi Arabia over the study period were relatively low (Table 1). In 2018, only 24 pertussis cases were reported, with an incidence rate of 0.1 cases per 100,000 persons. However, in 2019, there was a remarkable increase in its incidence rates to 0.7 (95% CI: 0.68, 0.72), then a drop to 0.2 (95% CI: 0.19, 0.21) in 2020, and a decline to 0.1 cases per 100,000 persons in 2021. There was a significant difference in the average pertussis cases between different age groups (p value = 0.04). However, post hoc analysis revealed no statistical significance.

Cholera is considered an endemic in several countries with poor sanitation and inadequate hygiene [16]. The global burden of cholera disease is undetermined because most of the cases are not reported [17]. Cholera is infrequently reported in Saudi Arabia (Table 1). The cholera incidence rate was 0.2 (95% CI: 0.19, 0.21) in 2018, followed by an incidence decline to 0.1 (95% CI: 0.09, 0.11) in 2019. Cases dropped remarkably in 2020 and 2021, with a rate of 0.04 cases per 100,000 persons and a rate of 0.05 cases per 100,000 persons, respectively. During 2018–2019, cholera (O1) was the most

Table 4 Regression analysis of reported bacterial infectious disease trends over time

	Correlation coefficient	R^2 value	Standard error	*F* value	*p* value
Brucellosis	0.96	0.91	533.26	21.19	**0.04**
Pulmonary TB	0.81	0.65	280.02	3.78	0.19
Extra-pulmonary TB	0.68	0.47	118.44	1.76	0.32
Salmonella infection	0.19	0.04	560.62	0.07	0.81
Typhoid–paratyphoid fever	0.55	0.31	158.76	0.88	0.44
Meningitis meningococcal	0.95	0.89	0.59	17.29	**0.05**
Meningococcemia	0.32	0.10	0.95	0.22	0.68
Meningitis—pneumococcal	0.88	0.78	7.51	7.03	0.12
Meningitis—HIB	0.94	0.88	1.83	14.34	0.06
Meningitis—other	0.89	0.80	33.33	7.86	0.11
Pertussis	0.17	0.03	102.81	0.06	0.83
Shigellosis	0.61	0.37	16.74	1.17	0.39
Cholera—O1	0.95	0.90	7.25	18.67	**0.05**
Cholera—O139	0.26	0.07	1.18	0.14	0.74
Cholera—non-O1 non-O139	0.38	0.15	3.07	0.34	0.62
Non-neonatal tetanus	0.56	0.31	7.11	0.89	0.44
Neonatal tetanus	0.15	0.02	3.02	0.05	0.85
Leprosy	0.60	0.36	6.36	1.11	0.40
HIB: encephalitis	0.77	0.60	0.39	3.00	0.23
Syphilis	0.26	0.07	5.32	0.14	0.74
Diphtheria	0.67	0.45	0.87	1.67	0.33

EPTB extrapulmonary tuberculosis, *HIB Haemophilus influenzae* type B

reported serotype, followed by cholera (non-O1 and non-O139). However, during 2020–2021, cholera (non-O1 and non-O139) became the most reported serotype. Cholera (O139) is rarely reported in Saudi Arabia. A significant decreasing trend in cholera O1 incidence rate was observed (p value = 0.05). There was a significant difference in the average cholera (non-O1 and non-O139) cases between different age groups (p value = 0.01). However, post hoc analysis revealed no statistical significance.

Tetanus is an acute life-threatening disease acquired through infection of a cut or wound with the exotoxin produced by the bacterium *Clostridium tetani* (*C. tetani*) [18]. Neonatal tetanus is a severe form of generalized tetanus that affects newborn infants through contaminated umbilical stumps or because the mother has not been sufficiently immunized [19]. Tetanus cases reported in Saudi Arabia range from 10 to 30 cases annually (Table 1). About 2–8 of these cases were reported in neonates. The tetanus (including neonatal tetanus) incidence rate increased to 0.1 cases per 100,000 persons in 2019, compared with 0.05 in the previous year. In 2020, the tetanus rate dropped to 0.05 cases per 100,000 persons and continued to decrease to 0.03 in 2021. Generally, tetanus affected non-Saudis more significantly than Saudi citizens (p value = 0.03). There was a significant difference in the average non-neonatal tetanus cases between different age groups (p value < 0.01). However, post hoc analysis revealed no statistical significance.

Leprosy, or Hansen's disease, is a chronic skin and peripheral nerve infection caused by *Mycobacterium leprae* (*M. leprae*) [20]. Leprosy affects around 20 persons in Saudi Arabia each year (Table 1). Throughout the study period (2018–2021), the highest number of leprosy cases was reported in 2018 (a rate of 0.1 cases per 100,000 persons), while the lowest was reported in 2020 (a rate of 0.04 cases per 100,000 persons). In 2021, 20 leprosy cases were reported, with a rate of 0.06 cases per 100,000 persons. Leprosy was highly significant in non-Saudi than in Saudi citizens (p value = 0.01). Most leprosy cases affected males more significantly than females (p value = 0.04). There was a significant difference in the average leprosy cases between different age groups (p value < 0.01). However, post hoc analysis revealed no statistical significance.

Haemophilus influenza disease is an infection caused by several recognized strains of *H. influenzae*, but the most common one is HIB. *H. influenzae* is responsible for numerous localized and invasive infections that often cause severe complications, particularly among infants and children [21]. In Saudi Arabia, the Saudi epidemiological surveillance only reports the number of meningitis and encephalitis cases caused by HIB. Other invasive HIB cases were not reported. Invasive HIB (encephalitis) is extremely rare in Saudi Arabia. In 2018, two cases of invasive HIB (encephalitis) were reported, with a rate of 0.01 cases per 100,000 persons. During 2019–2021, only one case of invasive HIB (encephalitis) was reported in each year.

Syphilis is a chronic sexually transmitted disease (STD) caused by the Spirochaete bacterium *Treponema pallidum* (*T. pallidum*) [22]. Syphilis is not common in Saudi Arabia. As shown in Table 1, no syphilis infections were reported in 2018, 2019, and 2021; however, nine cases were reported in 2020, with a rate of 0.03 cases per 100,000 persons.

Diphtheria is an acute bacterial infection caused by toxigenic *Corynebacterium diphtheriae* (*C. diphtheriae*) [23]. In Saudi Arabia, diphtheria infection is infrequent (Table 1), due to vaccination programs. In 2018, only one case of diphtheria was reported in Saudi Arabia, two cases were reported in 2019 (a rate of 0.01 cases per 100,000 persons), and none were reported in both years 2020 and 2021.

DISCUSSION

Bacterial infections have a significant impact on human health; they can cause severe morbidity and mortality, particularly in susceptible populations such as children, infants, the elderly, and those with compromised immune systems. Due to the costs of diagnosis, treatment, and prevention, they can also represent a considerable economic burden [24]. Saudi Arabia faces various challenges in preventing and controlling bacterial infectious diseases due to its large and diverse population of about 31 million (≈ 18 million Saudi and 13 million non-Saudi citizens) people who live in different regions and conditions. Each year, a large mass gathering occurs in Makkah and Madinah, Saudi Arabia, when over 5 million people from all over the world arrive in the country to perform Hajj and Umrah [5]. Supposedly, any inappropriate prescription of antibiotics during Hajj and Umrah would raise antibiotic resistance globally [25]; hence, huge efforts are being exerted to reduce the overuse of antibiotics during these events [26].

In Saudi Arabia, brucellosis was the most reported bacterial infectious disease between 2018 and 2019. The high rate of brucellosis in Saudi Arabia is probably due to the cultural practice of consuming unpasteurized raw milk from sheep and camels and direct contact with infected animals [27]. Numerous studies have investigated the risk factors associated with the high prevalence of brucellosis in Saudi Arabia. These studies revealed that most brucellosis patients had a history of direct animal contact or ingestion of raw milk products. Veterinary practitioners and cattle owners have an increased risk of infection [27–30]. However, our study revealed that brucellosis incidence rates show a significant decreasing trend. This reduction indicates that Saudi Arabia succeeded in preventing and eliminating Brucella infection risk factors. Nevertheless, Saudi Arabia still needs to undertake an organized national brucellosis eradication program to eradicate the disease effectively. Numerous strategies should be implemented to eliminate brucellosis, including animal vaccination programs, increasing disease awareness, debunking unpasteurized milk myths, applying food safety measures by avoiding undercooked meat and unpasteurized dairy products, and maintaining good hygiene. Moreover, brucellosis is one of the common laboratory-acquired infections, and it is important to establish a comprehensive biosafety system in laboratories to eliminate the risk of laboratory-acquired brucellosis [31].

During the Hajj and Umrah seasons, upper respiratory tract infections are particularly the most common infectious diseases occurring, followed by gastrointestinal infections [25]. Saudi Arabia faces a challenge in the spread of TB as it is highly contagious and difficult to control, especially during mass gatherings like Hajj and Umrah. Eradicating TB infection will require global efforts to maintain and strengthen the current TB control programs while focusing on identifying and treating latent TB infections [32]. Our study determined that TB incidence rates decreased slightly from 2018 to 2021; however, no significant decreasing trend was observed. Also, the results show that pulmonary TB is significantly higher among non-Saudi, and most of the TB infections (both pulmonary TB and EPTB) affect adults more than children and the elderly in Saudi Arabia. Promoting disease awareness, early detection, and appropriate management of disease is crucial. In June of 2016, Saudi Arabia adopted the WHO's strategic plan to eradicate TB infections (i.e., End-TB strategy). This strategy aims to end the global TB epidemic to reach a world free of TB, with zero deaths, zero diseases, and zero suffering from TB [33]. Hence, Saudi Arabia's Ministry of Health launched the National Tuberculosis Program (NTP), which achieved a reduction in the rate of TB cases and the TB death rate by 21 and 12.3%, respectively, in 2021 compared to 2015, with a success rate of TB treatment that reached 89.5% during 2021 [34].

Salmonellosis is one of the top bacterial infectious diseases reported in Saudi Arabia. However, there was a remarkable decline in salmonellosis incidence in 2020, mainly due to the cancellation of Hajj and Umrah during the COVID-19 pandemic with quarantine measures and travel restrictions. Salmonellosis is particularly prevalent during the Hajj and Umrah seasons, as demonstrated in previous studies [35, 36]. Salmonellosis affects Saudi citizens more significantly than non-Saudi citizens and children under the age of 5 more significantly than other age groups. Importantly, drug-resistant salmonella infections pose a serious threat to human health. Consequently, appropriate management of salmonellosis and proper prescription of antibiotics, especially during Hajj and Umrah, is urgently needed. Preventive measures help to reduce the chances of getting food-borne salmonellosis. The United States Food and Drug Administration (FDA) has published guidelines for the Food Safety and Inspection Service to control measures for all stages of the food chain, from agricultural production to food preparation at home [37].

Some bacterial infectious diseases are rarely reported in Saudi Arabia due to vaccination programs. The Saudi national immunization schedule includes three doses of Diphtheria Tetanus and Pertussis (DTaP) vaccine routinely administrated at 2, 4, and 6 months of age, followed by boosters at the age of 18 months and preschool entry. A complete DTaP vaccine series is proven to prevent diphtheria, tetanus, and pertussis infections [38]. Consequently, the incidence rate of these infections is relatively rare. Zero cases of diphtheria have been reported in 2020 and 2021. Most tetanus cases, including neonatal tetanus, affected non-Saudi citizens more significantly than Saudi citizens; this could be due to insufficient vaccination or inadequate immunization. Increasing awareness of tetanus disease and immunization is required, especially among construction workers. Furthermore, since the introduction of the HIB vaccine in the early 1990s [39], the conjugated HIB vaccine has become a routine in the Saudi national immunization schedule in the early 2000s [40]. Children are routinely vaccinated with HIB vaccine at 2, 4, 6, and 18 months of age [38]. Consequently, invasive HIB, including encephalitis and meningitis, are rarely reported in Saudi Arabia. Moreover, the routine administration of the Meningococcal Conjugate Quadrivalent vaccine at 9 and 12 months of age [38] has contributed to the low incidence of disease in Saudi Arabia. Vaccination programs during the Hajj and Umrah seasons have contributed to minimizing the spread of infectious diseases in Saudi Arabia. Meningococcal meningitis outbreaks have been reported during Hajj and Umrah. Therefore, Saudi Arabia has introduced the Meningococcal Quadrivalent (ACYW) vaccine as one of the requirements for all pilgrims to perform Hajj [41]. However, the significantly increasing trend in meningococcal meningitis incidence rate needs to be monitored closely in Saudi Arabia, and setting restricted guidelines for managing and preventing meningitis outbreaks is necessary.

One of the essential epidemiological factors that influence infectious diseases is sex differences. Several factors may influence the distribution pattern of bacterial infections between different sexes. Previous studies have demonstrated an apparent sexual dimorphism in bacterial infections in animals and humans [42]. Sexual dimorphism has been shown to influence susceptibility to conditions, infectious disease pathogenesis, disease frequency and severity, and response to therapy and vaccinations [43]. The hormonal, genetic, and environmental differences have mainly been attributed to sexual dimorphism in bacterial infections [44]. In Saudi Arabia, males were more significantly affected by brucellosis, tuberculosis (pulmonary TB and EPTB), non-neonatal tetanus, and leprosy infections than females. The distribution pattern of the Saudi Arabian population between different sexes and the high percentage of the male population (≈ 60%) might contributed to the increased incidence of some bacterial infectious diseases among males [45]. Furthermore, the lifestyle and environmental factors of males might influence the distribution pattern of these bacterial infections.

The causality of reported infections has not been determined in the Saudi epidemiological surveillance data. To illustrate, a significant decreasing trend in the cholera O1 incidence rate was observed in our study. However, cholera is considered a neglected and underreported infectious disease. Therefore, further investigation is needed to determine the causality of this decreasing trend. Implementing an improved public health surveillance system is necessary to overcome challenges associated with underreporting communicable diseases. Well-conducted surveillance relies on criteria that include simplicity, flexibility, timelines, data quality, acceptability, sensitivity, representativeness, and reliability [9]. The specificity of Saudi disease surveillance should be improved since some diseases are not specified or not included in the surveillance system. Among the reported bacterial infectious diseases, "Meningitis- other" is not specified, while the incidence rate is higher than the other reported meningitis rates. The most common invasive diseases caused by *H. influenzae*, such as pneumonia, bloodstream infection, and infectious arthritis, are not included in the Saudi surveillance system. Moreover, the Saudi surveillance system does not include the bacterial pathogens involved in global infection-related mortality.

CONCLUSIONS

Monitoring the incidence and epidemiology of bacterial infectious diseases is an initial core step toward public health goals. Our study shows that brucellosis, tuberculosis, and salmonellosis were the most frequently reported bacterial contagious diseases in Saudi Arabia between 2018 and 2021. The significantly increasing trend in the incidence rate of meningococcal meningitis is quite concerning, especially during the Hajj and Umrah seasons. Essential strategies to prevent such infections are crucial and include raising awareness regarding disease transmission, increasing the rate of vaccination, applying food-safety measures by avoiding the consumption of undercooked meat and unpasteurized dairy products and improving access to safe drinking water, in addition to facilitating access to appropriate antibiotic therapy for treating these infections. Other strategies are also critical to decrease the burden and the consequences of bacterial infections and the rate of bacterial resistance, including improving the diagnostic infrastructure and implementing appropriate infection control and antimicrobial stewardship measures. The future perspective of this research is enhancing disease surveillance reporting by including different variables, such as the source of infection, travel history, hospitalization, and mortality rates. Furthermore, improving the sensitivity and specificity of surveillance data and focusing on the mortality associated with bacterial pathogens to identify the most significant threats and set a public health priority.

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Declarations

Conflict of Interest. Nada Alhumaid, Areej Alajmi, Nada Alosaimi, Maryam Alotaibi, Thamer Almangour, Majed Nassar, Zias Memish, Abdulwahab Binjomah, Amed Al-Jedai, Abdulaziz Almutairi, Saeed Algarni, Noura Alshiban, Munirah Aleyiydi, Abdulkader Tawfik, Atef Shibl, and Essam Tawfik declare that they have no financial or non-financial conflicts of interest.

Ethical Approval. This study is based on previously collected data and does not contain any new data that involved human participants or animals performed by any of the authors.

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